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EXAMINER

SODERQUIST, ARLEN

ART UNIT	PAPER NUMBER
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1743

DATE MAILED: 12/12/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

# Office Action Summary

Application No.

09/508,775

Applicant(s)

MATTIASSEN ET AL.

Examiner

Arlen Soderquist

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

## Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☐ Responsive to communication(s) filed on \_\_\_\_.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 1-10 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-10 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

## Priority under 35 U.S.C. §§ 119 and 120

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_.
  - ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 13) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.
- a) ☐ The translation of the foreign language provisional application has been received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

## Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 5.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other:

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1. Claim 2 is objected to because of the following informalities: the abbreviation "PEGDGE" is nonstandard and should be replaced with the chemical that it represents.

Appropriate correction is required.

2. Claim 10 provides for the use of a sensor according to claim 6, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

3. Claim 6 is rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd. v. Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

4. Claims 1-10 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949). In the present instance, claims 1 and 6 recite the broad recitation "at least 90%", and the claims also recite at least 95%, 97% and 99% which are narrower statements of the range/limitation. Claim 3 recites the broad recitation "containing a crosslinking agent", and the claim also recites "glutaraldehyde" which is the narrower statement of the range/limitation. Claim 5 recites the broad recitation "a thiol comprising 3-25 carbon atoms", and the claim also recites "1-dodecanethiol" which is the narrower statement of the range/limitation. In claim 1, it

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is not clear if additional structure such as a second piece of metal that is separated from the first piece of metal by a defined distance is required to form a capacitance sensor or if applicant is really claiming an electrode for use in a capacitance sensor. Claim 6 is also dependent upon itself. Claim 7 is not in proper Markush format in that the group is not closed and it is not clear what constitutes "functional derivatives thereof having equivalent binding characteristics". In claim 8 "said affinity groups"(subparagraph a)) does not have proper antecedent basis. In claim 8, the scope of "According to per se known methods" is not clear in that it does not set forth those methods which are included as known methods. In claim 8, the last part of the claim -- the calculating step -- is not optional for quantitatively determining the heavy metal ion.

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

6. Claims 1 and 3-10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hilpert (EP 263948) in view of Berggren and Fowlkes (US 5,935,823), Kay (US 5,498,538), Lopez (US 5,972,656) or Wylie (US 6,111,079). In the published application Hilpert teaches a biosensor. The biosensor comprises a reactive biochemical component, especially a phytochelatin peptide, immobilised on a transducer. Suitable transducers are field effect transistor units, with a layer of phytochelatin immobilised on the gate; piezoelectric crystals coated with a layer of immobilised phytochelatin; and optical conductors with a layer of immobilised phytochelatin. On contact with aqueous solutions of heavy metal ions, complexes with the phytochelatin lead to a change in the transducer output, so that the devices provide a rapid means of analysis of heavy

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metal ions. The phytochelatins are being treated as functional derivatives of the specific sequences claimed in claim 7. Hilpert does not teach the specifically claimed steps of how the peptides are immobilized on the transducers.

In the paper Berggren teaches capacitance measurements of antibody-antigen interactions in a flow system. Capacitive immunosensors were made by coupling monoclonal antibodies to thioctic acid, which had self-assembled on a gold electrode. Surface areas that were not covered were plugged with 1-dodecanethiol to make the layer dense and insulating. See the experimental section on page 3652 for a full disclosure of the formation process. Cyclic voltammetry showed that the hexacyanoferrate redox reactions were blocked by this procedure. The capacitance of the electrode was evaluated from the current transients obtained when a potentiostatic step was applied. The immunosensor was placed in a flow system, and a capacitance decrease could be observed after injection of an unlabeled antigen. It was linear over almost three decades when plotted vs. the logarithm of the antigen concentration. Several analytes were determined with a detection limit of 1 pg/mL.

In the patent Fowlkes teaches heterofunctional binding fusion proteins termed totally synthetic affinity reagents (TSARS) that are concatenated heterofunctional polypeptides or proteins comprising at least two functional regions: a binding domain with affinity for a ligand that is characterized by 1) its strength of binding under specific conditions, 2) the stability of its binding under specific conditions, and 3) its selective specificity for the chosen ligand (see column 16, lines 1-5) and a second effector peptide portion that is chemically or biologically active. In one embodiment, the heterofunctional polypeptides or proteins further comprise a linker peptide portion between the binding domain and the second active peptide portion. The linker peptide can be either susceptible or not susceptible to cleavage by enzymatic or chemical means. Novel and/or improved heterofunctional binding reagents as well as methods for using the reagents for a variety of in vitro and in vivo applications are also disclosed. In column 5, lines 36-42 teach that the term phytochelatin was proposed for the major heavy metal binding peptides of higher plants [Grill et al., Science 230: 674 (1989)]. The structure of these small peptides was determined to be  $\text{NH}_3^+ - \gamma\text{Glu-Cys-}\gamma\text{Glu-Cys-}\gamma\text{Glu-Cys-}\gamma\text{Glu-Cys-Gly-COO}^-$  with

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minor components of  $(\gamma\text{Glu-Cys})_n\text{Gly}$  where  $n=3, 5, 6$  or  $7$ . The peptides were induced by and bound  $\text{Cd}^{++}$ ,  $\text{Cu}^{++}$ ,  $\text{Hg}^{++}$ ,  $\text{Pb}^{++}$  and  $\text{Zn}^{++}$ .

In the patent Kay has a disclosure that is similar to Fowlkes since they both claim benefit of the same patent application. Kay differs from Fowlkes as it discloses more peptides than Fowlkes.

In the patent Lopez teaches metal binding polypeptides which include an amino acid sequence coding for a variable region of a monoclonal antibody which immunoreacts with a mercury cation. The invention is also directed to fusion proteins which include a phage coat protein or portion thereof and the monoclonal antibody heavy chain variable region. The invention also provides bacteriophages which include the fusion protein in their coat. In addition, methods for detecting, removing, adding, or neutralizing mercuric cations in biological or inanimate systems through the use of the mercury binding polypeptides are provided. Column 4, lines 40-67 teach advantages that include a high specificity for the heavy metal. Column 5, lines 59-67 teach that these methods utilize features such as metal binding polypeptide immobilization, heavy metal immobilization, competitive binding, and means employing an oscillating probe, a micromagnetic probe and other physiochemical methods typically used to monitor antigen-antibody interactions. Column 6, lines 1-54 give more specific details on the detection methods.

In the patent Wylie teaches metal binding polypeptides which include an amino acid sequence coding for a light chain variable region of a monoclonal antibody capable of immunoreacting with a lead cation and nucleotides which include a nucleic acid sequence coding for the variable region are provided. The invention is also directed to fusion proteins and Fab fragments which include the light chain variable region. In addition, methods for detecting, removing, adding, or neutralizing lead cations in biological or inanimate systems through the use of the lead binding polypeptides are provided. Column 4, lines 31-61 teach advantages that include a high specificity for the heavy metal. Column 6, lines 7-56 teach that these methods utilize features such as metal binding polypeptide immobilization, heavy metal immobilization, competitive binding, and means employing an oscillating probe, a micromagnetic probe and other physiochemical methods typically used to monitor antigen-antibody interactions.

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It would have been obvious to one of ordinary skill in the art at the time the invention was made to immobilize the detection compounds of Hilpert through a process as taught by Berggren because of the ability to attach a complexing peptide to the metal and cover the surface of the metal with a compound that will block its interaction with a sample as taught by Berggren. It would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute the metal complexing peptides of Fowlkes, Kay, Lopez or Wylie or other well peptides and protein having the ability to bind heavy metals for the phytochelatin or Hilpert because of there equivalence as taught by Fowlkes and Kay or their known selectivity towards the metal as taught by Lopez or Wylie.

7. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. The additionally cited art relates to peptides having metal binding properties.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Arlen Soderquist whose current telephone number is (703) 308-3989. After about December 16, 2003, this number will change to (571) 272-1265 as a result of the examiner moving to the new USPTO location. The examiner's schedule is variable between the hours of about 5:30 AM to about 5:00 PM on Monday through Thursday and alternate Fridays.

For communication by fax to the organization where this application or proceeding is assigned, (703) 305-7719 may be used for official, unofficial or draft papers. When using this number a call to alert the examiner would be appreciated. Numbers for faxing official papers are 703-872-9310 (before finals), 703-872-9311 (after-final), 703-305-7718, 703-305-5408 and 703-305-5433. The above fax numbers will generally allow the papers to be forwarded to the examiner in a timely manner.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0661.



December 10, 2003

ARLEN SODERQUIST  
PRIMARY EXAMINER